

# **EXHIBIT 5**

UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF OHIO  
EASTERN DIVISION

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IN RE: NATIONAL PRESCRIPTION  
OPIATE LITIGATION | MDL No. 2804  
This document relates to: | Case No. 17-md-2804  
Jennifer Artz v. Endo Health | Judge Dan Aaron Polster  
Solutions Inc., et al. |  
Case No. 1:19-OP-45459 |  
Darren and Elena Flanagan v. |  
McKesson Corporation, et al. |  
Case No. 1:18-OP-45405 |  
Michelle Frost, et al., v. |  
Endo Health Solutions Inc., |  
et al. |  
Case No. 1:18-OP-46327 |  
Walter and Virginia Salmons, |  
et al., v. McKesson |  
Corporation, et al. |  
Case No. 1:18-OP-45268 |

VIDEOTAPED DEPOSITION OF  
DR. CHARLES VYVYAN HOWARD  
January 27, 2020  
Chicago, Illinois

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21 ALSO PRESENT:

22 Mr. Kevin Duncan, Videographer

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\* \* \*

1 windows of vulnerability, so the timing here is  
2 extremely important.

3 Q. And we'll get into the details of  
4 that during the course of the day, but let me  
5 just -- I think where you're going with this is  
6 am I correct that when you're looking at things  
7 that might affect the development of a fetus,  
8 timing of when the fetus is exposed to a  
9 substance is important?

10 A. Yes.

11 Q. Is it also the nature or type of  
12 substance that they're exposed to matters,  
13 right?

14 A. Clearly.

15 Q. Okay. And am I right that the  
16 duration of exposure will affect a fetus  
17 differently, short- versus long-term exposure  
18 during the pregnancy?

19 A. Again, it depends which windows of  
20 vulnerability it's moving through, but in the  
21 nervous system, for apoptosis, that's quite a  
22 protracted period.

23 Q. Okay. And so it can then, the  
24 duration can, not always, but can have an

1 impact on the fetus?

2 A. True.

3 Q. Okay. So we got timing, duration,  
4 nature -- you know, the type of substance --

5 A. Dose.

6 Q. We'll go through it, but -- I assume  
7 then that anything that the fetus is exposed to  
8 could potentially impact that fetus?

9 A. That's a very general statement.

10 Q. Right. But so anything the mom  
11 takes, whether it's drugs, what she eats,  
12 whether she's exposed to environmental hazards,  
13 maybe depending upon where she lives or works,  
14 all of those things could potentially impact  
15 the fetus, right?

16 A. Things -- yeah, things have a  
17 potential to impact the fetus, of course.

18 Q. Okay. Genetics would affect the  
19 fetus, right?

20 A. Genetics can have an effect, yes,  
21 all part of the mix.

22 Q. Do you consider yourself a leading  
23 world expert on how prescription opioid use  
24 impacts fetus's neurological development?

\* \* \*

1                   woman and determine what  
2                   else she was exposed to,  
3                   when, the dose, the  
4                   duration, the timing of a  
5                   lot of other exposures, that  
6                   by the scientific literature  
7                   we know, could actually have  
8                   an impact on the neurologic  
9                   and structural development  
10                  of fetuses."

11       BY MS. FUJIMOTO:

12               Q.       Is that accurate, Doctor, to your  
13       knowledge?

14               A.       The other factors could be  
15       contributory to the known exposure to opioids.

16               Q.       Right.

17               A.       Correct.

18               Q.       Okay. Thank you.

19                       Five minutes, let me see if we can  
20       get through this exhibit, and then we'll take a  
21       break, okay?

22               A.       Yes.

23               Q.       Going back to Exhibit 6, which is  
24       the e-mail traffic, let's see, the

\* \* \*

1 effect is large, you know.

2 Q. This is another paper that you cited  
3 to. I'll mark as Exhibit 10 to the  
4 deposition --

5 (Exhibit 10 marked for  
6 identification.)

7 BY MS. FUJIMOTO:

8 Q. -- by Gilardi: Will Widespread  
9 Synthetic Opioid Consumption Induce Epigenetic  
10 Consequences in Future Generations?

11 You recognize that?

12 A. I do.

13 Q. Okay. And it talks right upfront  
14 there in the first -- second sentence of the  
15 abstract. It says:

16 Both maternal and paternal  
17 transmission of phenotype across generations  
18 has been proved, demonstrating that parental  
19 drug history may have significant implications  
20 for subsequent generations.

21 Do you see that?

22 A. I do.

23 Q. All right. And so I take it you  
24 agree with me that a woman's genetics will

1 influence how the fetus is impacted by  
2 different exposures, whether it's opioids or  
3 not?

4 A. And I presume, also, if the father  
5 had been exposed that it might come from him as  
6 well. I mean, you know, that's a possibility.  
7 This is well-known.

8 Q. And so that was my second question.  
9 Not only the genetics of the mother,  
10 but the genetics of the baby's father is  
11 important in whatever effects opioid exposure  
12 might have on that fetus, right?

13 A. In the epigenetic influences, yeah.

14 Q. And so epigenetic inheritance that  
15 each baby gets from their parents, that can  
16 include not just prenatal exposure, but  
17 parental exposure too, right?

18 A. As illustrated in Figure 1.

19 Q. Yes.

20 Like it says here on page 2, under  
21 Molecular Mechanisms Underlying the Impact of  
22 Drugs, it says:

23 A family history of drug abuse  
24 correlates with increased risk of drug use in

1       offspring.

2                       Correct?

3           A.       Yes.

4           Q.       Okay.   So --

5           A.       Can you just show me exactly  
6       where --

7           Q.       Right here.

8           A.       There, yeah.

9           Q.       But we know that to be true, right?

10          A.       Yes.

11          Q.       And so if you're looking at women  
12       who have used prescription opioids, the use of  
13       a prescription opioid during pregnancy is not  
14       the only thing that is important, but her  
15       history of drug use would be important too,  
16       right, in terms of the impact on the fetus?

17          A.       It would -- I suspect that that is  
18       what a clinician would want to collect.

19          Q.       And every pregnant woman has  
20       different genetics and a different history as  
21       to whether that lot they used had a drug abuse  
22       history or never used a drug at all, right --

23          A.       Yes.

24          Q.       -- true?

1                   And then for each of those babies,  
2                   the genetics and the drug history of the father  
3                   comes into play as well because of this idea of  
4                   epigenetic modifications in the role of sperm  
5                   RNA.

6                   A.       Yes, but it is important not to lose  
7                   site of the fact that the genome of the fetus  
8                   is also being exposed, and that can cause these  
9                   effects as well.

10                  Q.       And so we have the genetics and drug  
11                  history use of the father, the genetics and  
12                  drug history use of the mother and the genetics  
13                  of the baby, right?

14                  A.       Correct.

15                  Q.       That are all important to whatever  
16                  impact might happen as a result of opioid  
17                  exposure?

18                  A.       That's correct.

19                  Q.       Okay.

20                         MS. FUJIMOTO:   Okay.   We need to  
21                         take a break.   We have to change tapes.

22                         THE WITNESS:   Oh, right.

23                         THE VIDEOGRAPHER:   Going off the  
24                         video at 12:30 p.m.

1 (Recess taken.)

2 A F T E R N O O N S E S S I O N

3 THE VIDEOGRAPHER: We are going back  
4 on the video record at 1:13 p.m. You may  
5 proceed.

6 BY MS. FUJIMOTO:

7 Q. Welcome back, Dr. Howard.

8 I want to stick with -- we ran out  
9 of time -- before we finished with exhibit, I  
10 think it would be 10. That's the Gilardi  
11 paper.

12 A. I have that.

13 Q. Okay. Great. Thank you.

14 If you would go to page 4 of that  
15 paper, and the section I want to ask you about  
16 is Consequences of Opioid Prenatal Exposure.

17 Do you see that?

18 A. Can you direct me to it?

19 Q. Right here.

20 A. There. Page 4. Oh, yes, sorry.  
21 It's in the big writing.

22 Q. The big, bold, black writing. Okay.

23 The last sentence of the first  
24 paragraph of that section says:

1                   Prenatal opioid exposure can induce  
2                   neonatal abstinence syndrome (NAS) in newborn  
3                   infants, but knowledge about its long-term  
4                   effects is limited.

5                   Do you agree with that?

6                   A.       We are going to find out more as  
7                   these children get older, so this is really one  
8                   of the reasons why we need to have a monitoring  
9                   committee to -- to study that, and learn more,  
10                  so that we can really understand the spectrum  
11                  of disease and the nature of disease.

12                  MS. FUJIMOTO:   Move to strike,  
13                  nonresponsive.

14                  BY MS. FUJIMOTO:

15                  Q.       Doctor, my question is do you agree  
16                  with the statement that:

17                         Knowledge about long-term effects of  
18                         opioid exposure, prenatal opioid exposure is  
19                         limited.

20                  Do you agree with that?

21                  A.       It isn't full -- I mean we don't  
22                  have full information, so --

23                  Q.       Okay.

24                  A.       -- from that point of view, it is

1 limited, yes.

2 Q. Okay. And if you go down then to  
3 probably three quarters of the way down that  
4 next paragraph, the words "Indeed," the  
5 sentence starts with "Indeed."

6 Do you have that?

7 A. I do.

8 Q. Indeed, despite multiple efforts  
9 aiming at modeling the contributions of  
10 maternal opioid dose and of the concurrent  
11 exposure to other medications or illicit drugs,  
12 the results remain so far inconclusive.

13 Do you agree with that statement?

14 A. That is inconclusive with respect to  
15 knowledge of long-term effects.

16 Q. Um-hmm.

17 A. Well, I'm going to defer this to  
18 Dr. Anand anyway. This is more -- the clinical  
19 picture is definitely his specialty. I am  
20 trying to give the Court an understanding of  
21 the process, the mechanism.

22 Q. So does that mean you don't agree or  
23 disagree with the statement that the  
24 contributions of maternal opioid dose and of

1 the concurrent exposure to other medications or  
2 illicit drugs remain inconclusive?

3 A. I think they remain incomplete and  
4 that that information is still being collected,  
5 particularly as these cohorts get older.

6 The information we do have at the  
7 minute is that as they get older, the  
8 discrepancy between the exposed and nonexposed  
9 controls is increasing.

10 Q. If you go to the right-hand column,  
11 first full paragraph, they write:

12 Regarding the long-term consequences  
13 of in utero opioid exposure, clinical studies  
14 in humans are extremely complicated by the huge  
15 amount of variables, in paren, (i.e., doses and  
16 length of treatment) and of concurring risk  
17 factors that are often present, such as  
18 polysubstance use, stability, mother-child  
19 interaction, et cetera.

20 Do you agree with that statement?

21 A. I agree that it is complicated, yes.

22 Q. And if you go down to the bottom of  
23 that column, last sentence of the second to the  
24 last paragraph, they say:

1 Collectively, however, these data  
2 must be taken with caution due to the  
3 heterogeneity of prenatal drug exposure and the  
4 difficulty to disassociate opioid effects from  
5 other risk factors to which they are often  
6 associated.

7 Do you agree with that statement?

8 A. Yeah, well, scientists always take  
9 data with caution in complex cases, but I don't  
10 think that the author is trying to argue that  
11 we shouldn't collect it.

12 Q. I'm not suggesting that's what  
13 they're trying to say.

14 Do you agree that there is profound  
15 heterogeneity between prenatal drug exposure  
16 and that it is difficult to parcel out the  
17 effects of the opioids from all the other  
18 substances and risk factors that are often  
19 present?

20 A. As I've already stated on the  
21 record, these can be contributory factors, but,  
22 in these cases, what we do know is that there  
23 has been exposure to opioids and these children  
24 get withdrawal symptoms, which, if they're

1 treated postnatally with opioids, respond. So  
2 that's proof that it is the opioids that's  
3 causing their problem at that time, and we have  
4 a diagnosis.

5 So it's complicated because there  
6 are many factors, but what we do know in these  
7 cases is that opioids are implicated, and there  
8 may be other contributory factors.

9 Q. You do understand that the term  
10 "neonatal abstinence syndrome" can be used and  
11 diagnosed with relation to exposure to drugs  
12 other than opioids, don't you?

13 A. Yes, I do.

14 Q. Okay. And so you agree that the  
15 data show significant variability in the use of  
16 a variety of different substances, opioids,  
17 benzodiazepines, alcohol, tobacco, all kinds of  
18 things --

19 A. Yeah.

20 Q. -- that it's difficult to parcel out  
21 the effect of the opioid from the effect of  
22 other substances that can cause NAS --

23 A. But --

24 Q. -- or other substances that can

1       cause other cognitive problems down the road?

2           A.       But, if the child responds to opiate  
3       therapy to reduce its symptoms, withdrawal  
4       symptoms, then that simplifies the question  
5       quite a lot. Clearly, the opiates will have  
6       been -- because if the child was addicted to  
7       something else, it wouldn't respond necessarily  
8       to opioid therapy.

9           Q.       Including benzos and other  
10       substances?

11          A.       That might help.

12          Q.       Are you sure?

13          A.       Hmm?

14          Q.       I mean, are you sure that --

15          A.       That is -- I am not involved in  
16       treating children, but if they respond  
17       specifically to opioids, that would indicate  
18       that there has been opioid exposure.

19                 But, again, this is something I  
20       think that Dr. Anand will address and --

21          Q.       Right. So you don't have expertise  
22       in the area of NAS treatment?

23          A.       I do not.

24          Q.       Okay. Do you have any knowledge as

1 to whether NAS symptoms can resolve without  
2 opioid treatment?

3 A. They can. Not all children are  
4 treated with opioids --

5 Q. Right.

6 A. -- postnatally.

7 Q. So for those NAS babies who are  
8 diagnosed with NAS but aren't treated with  
9 opioids, how do you know -- how can you then  
10 confirm that their symptoms were attributed  
11 only to opioids, and not something else like  
12 benzodiazepines?

13 A. Well, we have the prescription  
14 history that they have been taking opioids, so  
15 they will be having an effect. And the other  
16 thing is they can be contributory effects, but,  
17 as I understand it, there has to be inadequate  
18 dose given to precipitate NAS in these  
19 children.

20 Q. Okay. First question is:

21 You agree, though, then it's  
22 difficult to parcel out the other contributory  
23 effects that you've acknowledged?

24 A. To actually quantify them.

1           Q.       Right, to parcel the amount and  
2 understand whether or not they could have a  
3 role and to what extent?

4           A.       Well, you would be able to take a  
5 history presumably.

6           Q.       Right.

7           A.       But that's, again, a clinical  
8 question. I think I've not been involved in  
9 trying to elucidate those problems. Dr. Anand  
10 presumably has.

11          Q.       Okay. So you don't have an opinion  
12 with respect to women who have both a  
13 prescription for opioids during pregnancy but  
14 also have reported history in the medical  
15 records of using benzodiazepine or other  
16 substances?

17          A.       I think that -- my opinion is that  
18 these children have been diagnosed by clinical  
19 attendants to have NAS, and that they have a  
20 history of opioids, and that's what I'm trying  
21 to inform the Court about is how  
22 that damage -- any damage could have been  
23 caused.

24          Q.       But you're acknowledging that other

1 things can cause damage?

2 A. It's complicated, yes.

3 Q. Yes, okay.

4 And you mention -- you've mentioned  
5 a few times that the fact that a baby is  
6 diagnosed with NAS confirms for you that they  
7 had adequate exposure to opioids.

8 A. That is the -- that is the effect  
9 that I'm basing my opinion on, that any damage  
10 for -- or a proportion, say, of the damage they  
11 have suffered could be through a mechanism  
12 which affects apoptosis.

13 Q. And so what dose is an adequate dose  
14 in your view?

15 A. One enough to produce NAS.

16 Q. And so if the baby is not diagnosed  
17 with NAS, they didn't have an adequate dose?

18 A. I think that opioid exposure without  
19 NAS does occur -- well, we know it occurs, and  
20 I think that they could be damaged as well. I  
21 don't think you have to have NAS to have  
22 affected apoptosis.

23 You know, as I told you before the  
24 break, this is of massive doses, massive doses.

1 I can give you -- I can give you an example of  
2 the susceptibility of the fetus to -- and the  
3 exquisite sensitivity that Professor Soto had  
4 down in Tufts. She's exposed pregnant rats to  
5 Bisphenol A and estrogen.

6 Q. Right, and so --

7 A. Can I just finish?

8 Q. Sure.

9 A. And this was at 1/250 thousandths  
10 of the dose you're required to produce an  
11 effect in an adult, and it produced a massive  
12 obvious change, naked-eye in the microscope  
13 change, to the breast tissue which was  
14 subsequently concerned to be malignant, so --  
15 premalignant.

16 So that's an example is that the  
17 fetus is working with cell-signaling molecules  
18 at parts per trillion, and they are  
19 physiologically active at that level, and we're  
20 putting in massive boluses of cell-signalling  
21 molecules, which in evolution, they've -- you  
22 know, they don't know how to cope with them  
23 basically. That's the problem.

24 It is this exquisite sensitivity to

1 the cell-signalling environment in the fetus,  
2 produces completely different effects than it  
3 would in an adult.

4 Q. Okay. So the question is:

5 Given this profound or this massive  
6 exposure, nonetheless, there are babies born  
7 who are not diagnosed with NAS, babies born  
8 that -- to mothers who have used opioids,  
9 right?

10 A. Yes.

11 Q. And is it your testimony, then, that  
12 even those babies that haven't been diagnosed  
13 have been harmed by the opioid exposure?

14 A. So this case here is dealing with  
15 babies that have had NAS diagnosed, and that's  
16 what I'm addressing.

17 Now, all the things we have been  
18 talking about for the last hour or two,  
19 polymorphisms, the genetics of the mother and  
20 the father, the complexity of cell signaling,  
21 dimerization, all these things mean that there  
22 will be a variable response --

23 Q. Right.

24 A. -- accepted.

1 Q. Right.

2 A. But we are dealing with very high  
3 doses of cell-signalling molecules which are  
4 known to be able to induce apoptosis.

5 So I don't -- I would not rule out  
6 damage with opioid exposure which doesn't  
7 produce NAS.

8 Q. Because given the high variability  
9 of, if not -- even more than variable, but  
10 individual fetal response to drug exposure,  
11 there can be harm in the setting of no  
12 diagnosis is your point?

13 A. Of NAS.

14 Q. Yeah. Right.

15 A. Absolutely.

16 Q. Okay. And there can be harm to  
17 fetuses that don't have NAS -- or have not been  
18 diagnosed with NAS, there can be harm caused to  
19 them developmentally or otherwise by the use of  
20 other drugs and substances by the mother,  
21 right?

22 A. Certainly that could happen.

23 Q. Okay. And, then, so for the mothers  
24 that used both opioids and other substances,

1     there will be individual and variable effects  
2     of each of those substances in different ways  
3     on each fetus, right?

4             A.     Yes, unpredictably and different.

5                     But with massive doses, some of  
6     these processes, such as cell migration and  
7     apoptosis, are very, as I've tried to explain,  
8     susceptible to high-dose effects because they  
9     are relying on a balance of very low dose cell  
10    signalling in the physiological state. So that  
11    is why I think that harm could occur at doses  
12    that don't produce FAS [sic].

13                             (Exhibit 11 marked for  
14                             identification.)

15                     MS. FUJIMOTO: I will mark as  
16     Exhibit 11 to the deposition the paper that  
17     you cited and relied upon by Susan  
18     Robinson, 2002, about the Effects of  
19     Perinatal Buprenorphine in Methadone  
20     Exposures on Striatal Cholinergic Ontogeny.

21                             You see that, Doctor?

22             A.     Yes.

23             Q.     Okay. And this is a study that was  
24     done on buprenorphine and methadone, both of

\* \* \*

1 Q. Okay.

2 A. I don't think I actually edited that  
3 chapter, by the way.

4 Q. Okay. Let's see about the next  
5 chapter.

6 So if you go toward the end of  
7 Exhibit 12, page through a few, and there is a  
8 chapter on Clinical Teratology.

9 A. Yes.

10 Q. Do you have it?

11 A. I do.

12 Q. Okay. That -- it would be page 147  
13 of this book chapter and the second paragraph.

14 A. Yes.

15 Q. It says:

16 Susceptibility to teratogenic agents  
17 depends on the combination of several factors  
18 including the genotype of the mother and/or of  
19 the fetus, dosage, the gestational period at  
20 exposure, pharmacokinetics and pharmacodynamics  
21 of the substance.

22 Do you agree with that?

23 A. Well, we discussed most of that  
24 already, and yes, that's a statement of fact.

\* \* \*

1 various exposures, whether it's multiple drug  
2 exposure, maternal incarceration, complex or  
3 violent family situations, nutritional  
4 deficiencies, and other transmission of  
5 infections, do you have an understanding that  
6 all of these factors can impact the post-birth  
7 development cognitive function and academic  
8 performance in babies that had been diagnosed  
9 with NAS when they were born?

10 MR. THOMPSON: Object to form,  
11 continuing objection, beyond scope.

12 THE WITNESS: I -- certainly from my  
13 medical knowledge, all of those could  
14 potentially impact on a child.

15 MR. THOMPSON: Could I borrow a  
16 Post-it Note?

17 MS. FUJIMOTO: Sure.

18 MR. THOMPSON: Maybe a couple.  
19 Thank you very much.

20 (Exhibit 14 marked for  
21 identification.)

22 BY MS. FUJIMOTO:

23 Q. Mark as Exhibit 14 to the deposition  
24 another paper you cited by Cheryl Broussard,

\* \* \*

1 to a specific reason, opioids were most  
2 commonly reported within surgical procedures,  
3 infections, chronic diseases, and injury  
4 sections of the questionnaire.

5 Do you see that?

6 A. Yes.

7 Q. And so this tells us that there's a  
8 large percentage of women who use opioids  
9 during pregnancy, who are prescribed opioids  
10 for reasons other than being addicted, right?

11 A. Yes.

12 Q. Okay. Let's see.

13 Okay. If you go to page 314.e6, or,  
14 you know, before you do this, let me just ask  
15 you this question:

16 When we talk about the percentage of  
17 women who are prescribed opioids for a reason  
18 other than addiction, are you familiar with  
19 ACOG guidelines as to the recommended practice  
20 of prescribing opioids in these non-addiction  
21 settings?

22 MR. THOMPSON: Objection, beyond  
23 scope.

24 THE WITNESS: I think I have read

\* \* \*

1 A. Yes.

2 Q. Well, then why wouldn't there be  
3 high variability?

4 A. The normal physiological condition  
5 in the developing fetus is very low doses which  
6 control cell signaling and, therefore, the  
7 likelihood of apoptosis in a particular cell or  
8 not. And this is a high-dose toxicology to the  
9 fetus when the mother takes therapy --

10 Q. Can you show me any paper that takes  
11 animal data and then confirms it in human  
12 epidemiologic studies that show a substance can  
13 cause birth defects and later cognitive  
14 neurodevelopmental effects, irrespective of  
15 timing of exposure?

16 A. Irrespective of timing of exposure?

17 Q. Irrespective of timing of exposure.

18 A. So we have talked about -- the first  
19 three weeks of human existence in the womb are  
20 refractory.

21 Q. Right.

22 A. Nothing much is going to happen.  
23 Then you move into another period up to week 12  
24 to week 16 where organogenesis is going on, and

\* \* \*

1 investigation. I have acknowledged that they  
2 can be contributory, and it is my opinion that  
3 the therapy that these ladies have been on, the  
4 maintenance therapy with opioids is sufficient  
5 to cause damage and lead to FAS -- NAS.

6 Q. And then let me ask you the bookend  
7 to that question, then:

8 We've talked about, and maybe we  
9 don't have to go through all of them, and there  
10 are a number of studies, that talk about  
11 post-birth factors that can affect NAS babies'  
12 development, cognitive abilities, academic  
13 performance, all of that, right? We have their  
14 environment, both family, geographic,  
15 socioeconomic, their education, their exposure  
16 to other bad substances after birth, all of  
17 which will impact how they perform on testing  
18 later on, right?

19 A. Yeah.

20 Q. Okay. And you -- I take it you've  
21 seen -- you cited to a number of those studies.  
22 You've cited to Desai, you've cited to Patrick,  
23 Conradt, Gee and Wolff and Yazdy.

24 Those are some of the papers that

1     you cited to that list a whole host of  
2     environmental variables after birth that impact  
3     a child's cognitive and neurobiologic  
4     development over time, right?  Yes?

5             A.     Yes.

6             Q.     So the question is:

7                     Have you done anything in your work  
8     to somehow quantify or assess the differential  
9     contribution of all of these post-birth factors  
10    that you acknowledge can impact the cognitive  
11    and neural performance of these NAS babies?

12            A.     Of course, there's a large  
13    proportion of these babies who were removed  
14    from their birth mother and fostered.

15            Q.     Yeah.

16            A.     And there's quite an interesting  
17    paper that's come out by Niga recently which  
18    assesses the progress of children who are still  
19    with their birth mother, while you might assume  
20    that conditions are not ideal with foster  
21    children, and they find no difference in  
22    outcome.

23            Q.     Um-hmm.

24            A.     So -- and then the other thing is

\* \* \*

1 to fetal life, right?

2 A. Yes, it has vulnerability which the  
3 adult doesn't have.

4 Q. And you agree that the brain has  
5 vulnerabilities in infancy as well?

6 A. Oh, yes. It's still in a very big  
7 state of flux.

8 Q. There you go.

9 And this is where it says:

10 For instance, early separation from  
11 caregivers, abuse, neglect or social  
12 deprivation in infancy or early childhood can  
13 produce enduring behavioral and neurocognitive  
14 deficits.

15 You agree with that, right?

16 A. Let me just read it again.

17 Q. For instance, early separation from  
18 caregivers, abuse, negligent or social  
19 deprivation in infancy or early childhood can  
20 produce enduring, behavioral and neurocognitive  
21 deficits.

22 And they cite to Carpenter and  
23 Stacks 2009 and Kreppner 2007.

24 MR. THOMPSON: Objection, beyond the

1 scope of his testimony.

2 BY MS. FUJIMOTO:

3 Q. Do you agree with that?

4 A. I think Dr. Anand will be able to  
5 address that.

6 Q. I assume you don't have any basis to  
7 disagree with it, though?

8 A. It's been published, and I don't  
9 disagree with it, but it's not in my scope.

10 Q. All right. Okay. Last one on this  
11 paper, 161 Conclusions and Future Directions.

12 Do you have it?

13 A. Yes, I do.

14 Q. It says:

15 Evolving experimental approaches  
16 have afforded us an increasingly nuanced view  
17 of the development of the brain's circuits as a  
18 protracted and even lifelong series of  
19 interrelated and partially overlapping  
20 iterative, biological processes that follow  
21 their own time courses across different brain  
22 regions.

23 That's accurate, isn't it?

24 A. Yes.

\* \* \*

1 reject the fact that there was a risk of  
2 teratogenic effect?

3 MS. FUJIMOTO: Object to form,  
4 foundation, documents speak for themselves,  
5 outside the scope of his review, and  
6 opinions based on prior testimony.

7 THE WITNESS: They didn't. By  
8 omission, they didn't mention any of this.

9 MR. THOMPSON: No further questions.  
10 Your witness.

11 Mr. Duncan, how much time do we  
12 have left?

13 THE VIDEOGRAPHER: Total elapsed  
14 time is 7 hours and 8 minutes.

15 MS. FUJIMOTO: I still had, what,  
16 32 minutes left?

17 THE VIDEOGRAPHER: 25 minutes.

18 FURTHER EXAMINATION

19 BY MS. FUJIMOTO:

20 Q. Okay. Doctor, just following up on  
21 your most recent testimony on a common mode of  
22 action, you were talking about the mu receptor  
23 and all that. I'm not going to go through it  
24 all; we have already been through it today, but

1 my question to you is when you reference a  
2 common mode of action, we have already  
3 discussed and you've confirmed that there would  
4 be no such effect before, say, three weeks,  
5 right, because mu opioid receptors and the  
6 other opioid receptors are not expressed in the  
7 fetal brain, right?

8 A. That's right, and that's the period  
9 of refractory.

10 Q. Exactly. So they can't have any  
11 teratogenic effects then, right?

12 A. I suppose they could have lethal  
13 effects, but they would not have teratogenic  
14 effects.

15 Q. Okay. And we have already discussed  
16 about the variability of impact depending upon  
17 timing of exposure, right?

18 A. Yes.

19 Q. Okay. Going back to the questions  
20 Mr. -- plaintiffs' counsel asked you regarding  
21 Olney and Creeley, do you remember those?

22 A. Vaguely.

23 Q. Okay. The two papers -- two of the  
24 several papers you and I talked about regarding

\* \* \*

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